Clinical trial results:
A Phase 2, Open-Label, Multicenter, Multi-cohort Study to Investigate the Safety and Efficacy of Sofosbuvir/Velpatasvir in Adolescents and Children with Chronic HCV Infection

Summary

EudraCT number	2016-002446-23
Trial protocol	GB BE Outside EU/EEA IT
Global end of trial date	26 February 2020

Results information

Result version number	v1
This version publication date	09 September 2020
First version publication date	09 September 2020

Trial information

Trial identification

Sponsor protocol code	GS-US-342-1143

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03022981
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001646-PIP01-14
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 February 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 November 2019
Global end of trial reached?	Yes
Global end of trial date	26 February 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the Pharmacokinetics (PK) Lead-in Phase was to evaluate the steady state PK and confirm the dose of sofosbuvir/velpatasvir (SOF/VEL) fixed-dose combination (FDC) in pediatric participants with chronic hepatitis C virus (HCV) infection. The primary objective of the Treatment Phase was to evaluate the safety and tolerability of SOF/VEL for 12 weeks in pediatric participants with chronic HCV.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements. This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 January 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 172
Country: Number of subjects enrolled	Italy: 24
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	Belgium: 5
Worldwide total number of subjects	216
EEA total number of subjects	44

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	114
Adolescents (12-17 years)	102
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 28 study sites in Belgium, Italy, the United Kingdom, and the United States. The first participant was screened on 26 January 2017. The final on-study visit occurred on 26 February 2020.

Pre-assignment

Screening details:

221 participants were screened.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	12 to < 18 Years Old

Arm description:

PK Lead-in Phase: Sofosbuvir/Velpatasvir (SOF/VEL) fixed-dose combination (FDC) 400/100 mg tablets or 2 * 200/50 mg tablets once daily for 7 days. Participants who completed the PK lead-in phase and other additional participants were enrolled into the treatment phase with no interruption of study drug administration until the appropriateness of the dose had been confirmed by PK and safety results from the PK lead-in phase.
Treatment Phase: SOF/VEL FDC 400/100 mg tablets or 2 * 200/50 mg tablets once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	SOF/VEL FDC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Granules
Routes of administration	Oral use

Dosage and administration details:

Tablets or oral granules administered once daily.

Arm title	6 to < 12 Years Old

Arm description:

PK Lead-in Phase: SOF/VEL FDC 200/50 mg tablets or oral granules once daily for 7 days. Participants who completed the PK lead-in phase and other additional participants were enrolled into the treatment phase with no interruption of study drug administration until the appropriateness of the dose had been confirmed by PK and safety results from the PK lead-in phase.
Treatment Phase: SOF/VEL FDC 200/50 mg tablets or oral granules once daily for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	SOF/VEL FDC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules, Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets or oral granules administered once daily.

Arm title	3 to < 6 Years Old

Arm description:

PK Lead-in Phase: SOF/VEL FDC 200/50 mg oral granules once daily for 7 days for participants who weighed ≥ 17 kg. SOF/VEL 150/37.5 mg FDC oral granules once daily for 7 days for participants who

weighed < 17 kg. Participants who completed the PK lead-in phase and other additional participants were enrolled into the treatment phase with no interruption of study drug administration until the appropriateness of the dose had been confirmed by PK and safety results from the PK lead-in phase. Treatment Phase: SOF/VEL FDC 200/50 mg oral granules once daily for 12 weeks for participants who weighed ≥ 17 kg. SOF/VEL 150/37.5 mg FDC oral granules once daily for 12 weeks for participants who weighed < 17 kg.

Arm type	Experimental
Investigational medicinal product name	SOF/VEL FDC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules, Tablet
Routes of administration	Oral use

Dosage and administration details:

Tablets or oral granules administered once daily.

Number of subjects in period 1	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old
Started	102	73	41
Completed	96	69	35
Not completed	6	4	6
Adverse Event	-	1	-
Withdrew Assent By Parent/Guardian	-	-	1
Investigator's Discretion	-	1	2
Non-Compliance With Study Drug	-	-	2
Lost to follow-up	6	2	1

Baseline characteristics

Reporting groups	
Reporting group title	12 to < 18 Years Old
Reporting group description:	
PK Lead-in Phase: Sofosbuvir/Velpatasvir (SOF/VEL) fixed-dose combination (FDC) 400/100 mg tablets or 2 * 200/50 mg tablets once daily for 7 days. Participants who completed the PK lead-in phase and other additional participants were enrolled into the treatment phase with no interruption of study drug administration until the appropriateness of the dose had been confirmed by PK and safety results from the PK lead-in phase. Treatment Phase: SOF/VEL FDC 400/100 mg tablets or 2 * 200/50 mg tablets once daily for 12 weeks.	
Reporting group title	6 to < 12 Years Old
Reporting group description:	
PK Lead-in Phase: SOF/VEL FDC 200/50 mg tablets or oral granules once daily for 7 days. Participants who completed the PK lead-in phase and other additional participants were enrolled into the treatment phase with no interruption of study drug administration until the appropriateness of the dose had been confirmed by PK and safety results from the PK lead-in phase. Treatment Phase: SOF/VEL FDC 200/50 mg tablets or oral granules once daily for 12 weeks.	
Reporting group title	3 to < 6 Years Old
Reporting group description:	
PK Lead-in Phase: SOF/VEL FDC 200/50 mg oral granules once daily for 7 days for participants who weighed ≥ 17 kg. SOF/VEL 150/37.5 mg FDC oral granules once daily for 7 days for participants who weighed < 17 kg. Participants who completed the PK lead-in phase and other additional participants were enrolled into the treatment phase with no interruption of study drug administration until the appropriateness of the dose had been confirmed by PK and safety results from the PK lead-in phase. Treatment Phase: SOF/VEL FDC 200/50 mg oral granules once daily for 12 weeks for participants who weighed ≥ 17 kg. SOF/VEL 150/37.5 mg FDC oral granules once daily for 12 weeks for participants who weighed < 17 kg.	

Reporting group values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old
Number of subjects	102	73	41
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	15	8	4
standard deviation	± 1.9	± 1.6	± 0.8
Gender categorical Units: Subjects			
Female	52	38	24
Male	50	35	17
Race			
Here, Not Permitted = local requirements did not permit collection of race or ethnicity information.			
Units: Subjects			
White	74	66	32
Black or African American	9	4	3
Asian	11	1	0
Other	5	2	5
American Indian or Alaska Native	2	0	0
Not Permitted	1	0	1
Native Hawaiian or Pacific Islander	0	0	0
Ethnicity			

Here, Not Permitted = local requirements did not permit collection of race or ethnicity information.			
Units: Subjects			
Hispanic or Latino	14	7	4
Not Hispanic or Latino	83	64	36
Not Permitted	5	2	1

Reporting group values	Total		
Number of subjects	216		
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	114		
Male	102		
Race			
Here, Not Permitted = local requirements did not permit collection of race or ethnicity information.			
Units: Subjects			
White	172		
Black or African American	16		
Asian	12		
Other	12		
American Indian or Alaska Native	2		
Not Permitted	2		
Native Hawaiian or Pacific Islander	0		
Ethnicity			
Here, Not Permitted = local requirements did not permit collection of race or ethnicity information.			
Units: Subjects			
Hispanic or Latino	25		
Not Hispanic or Latino	183		
Not Permitted	8		

End points

End points reporting groups

Reporting group title	12 to < 18 Years Old

Reporting group description:

PK Lead-in Phase: Sofosbuvir/Velpatasvir (SOF/VEL) fixed-dose combination (FDC) 400/100 mg tablets or 2 * 200/50 mg tablets once daily for 7 days. Participants who completed the PK lead-in phase and other additional participants were enrolled into the treatment phase with no interruption of study drug administration until the appropriateness of the dose had been confirmed by PK and safety results from the PK lead-in phase.
Treatment Phase: SOF/VEL FDC 400/100 mg tablets or 2 * 200/50 mg tablets once daily for 12 weeks.

Reporting group title	6 to < 12 Years Old

Reporting group description:

PK Lead-in Phase: SOF/VEL FDC 200/50 mg tablets or oral granules once daily for 7 days. Participants who completed the PK lead-in phase and other additional participants were enrolled into the treatment phase with no interruption of study drug administration until the appropriateness of the dose had been confirmed by PK and safety results from the PK lead-in phase.
Treatment Phase: SOF/VEL FDC 200/50 mg tablets or oral granules once daily for 12 weeks.

Reporting group title	3 to < 6 Years Old

Reporting group description:

PK Lead-in Phase: SOF/VEL FDC 200/50 mg oral granules once daily for 7 days for participants who weighed ≥ 17 kg. SOF/VEL 150/37.5 mg FDC oral granules once daily for 7 days for participants who weighed < 17 kg. Participants who completed the PK lead-in phase and other additional participants were enrolled into the treatment phase with no interruption of study drug administration until the appropriateness of the dose had been confirmed by PK and safety results from the PK lead-in phase.
Treatment Phase: SOF/VEL FDC 200/50 mg oral granules once daily for 12 weeks for participants who weighed ≥ 17 kg. SOF/VEL 150/37.5 mg FDC oral granules once daily for 12 weeks for participants who weighed < 17 kg.

Subject analysis set title	12 to <18 Years Old
Subject analysis set type	Full analysis

Subject analysis set description:

Treatment Phase: 2 * SOF/VEL 200/50 mg (adult and smaller size tablets based on swallowability assessment) once daily for 12 weeks.

Subject analysis set title	6 to <12 Years Old
Subject analysis set type	Full analysis

Subject analysis set description:

Treatment Phase: SOF/VEL FDC 200/50 mg oral granules once daily for 12 weeks.

Subject analysis set title	3 to <6 Years Old
Subject analysis set type	Full analysis

Subject analysis set description:

SOF/VEL FDC 150/37.5 mg oral granules once daily for 12 weeks for participants who weighed < 17 kg.

Primary: PK Lead-in Phase: AUCtau: Area Under the Plasma Concentration Versus Time Curve Over the Dosing Interval of Velpatasvir (VEL)

End point title	PK Lead-in Phase: AUCtau: Area Under the Plasma Concentration Versus Time Curve Over the Dosing Interval of Velpatasvir (VEL)[1]

End point description:

AUCtau is defined as concentration of drug over time (the area under the concentration versus time curve over the dosing interval). The Lead-in Phase Pharmacokinetic (PK) Analysis Set included all PK lead-in phase participants with available data who received at least 1 dose of study drug and whom at least one non-missing PK concentration data value is available from the PK Lead-in Phase intensive sampling.

End point type	Primary

End point timeframe:

Day 7: 0 (predose), 0.5, 1, 2, 3, 4, 6 (Cohorts 1 and 2 only), 8, and 12 hours postdose

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	17	18	
Units: hours*nanograms per millilitre (h*ng/mL)				
arithmetic mean (standard deviation)	4479.3 (± 2105.66)	3697.5 (± 1653.25)	4450.3 (± 3285.75)	

Statistical analyses

No statistical analyses for this end point

Primary: PK Lead-in Phase: AUCtau: Area Under the Plasma Concentration Versus Time Curve Over the Dosing Interval of Sofosbuvir (SOF)

End point title	PK Lead-in Phase: AUCtau: Area Under the Plasma Concentration Versus Time Curve Over the Dosing Interval of Sofosbuvir (SOF)[2]

End point description:

AUCtau is defined as concentration of drug over time (the area under the concentration versus time curve over the dosing interval). Participants in the Lead-in Phase PK Analysis Set with available data were analyzed.

End point type	Primary

End point timeframe:

Day 7: 0 (predose), 0.5, 1, 2, 3, 4, 6 (Cohorts 1 and 2 only), 8, and 12 hours postdose

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	17	17	
Units: h*ng/mL				
arithmetic mean (standard deviation)	3020.1 (± 1162.56)	1764.5 (± 690.12)	3306.2 (± 3499.49)	

Statistical analyses

No statistical analyses for this end point

Primary: PK Lead-in Phase: AUCtau: Area Under the Plasma Concentration Versus Time Curve Over the Dosing Interval of GS-331007 (Metabolite of SOF)

End point title	PK Lead-in Phase: AUCtau: Area Under the Plasma Concentration Versus Time Curve Over the Dosing Interval of

	GS-331007 (Metabolite of SOF)[3]

End point description:

AUCtau is defined as concentration of drug over time (the area under the concentration versus time curve over the dosing interval). Participants in the Lead-in Phase PK Analysis Set with available data were analyzed.

End point type	Primary

End point timeframe:

Day 7: 0 (predose), 0.5, 1, 2, 3, 4, 6 (Cohorts 1 and 2 only), 8, and 12 hours postdose

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	17	18	
Units: h*ng/mL				
arithmetic mean (standard deviation)	13852.9 (± 3565.85)	9913.8 (± 3071.79)	11604.0 (± 2732.57)	

Statistical analyses

No statistical analyses for this end point

Primary: Treatment Phase: Percentage of Participants Who Discontinued Study Drug Due to Any Treatment-Emergent Adverse Event (TEAE)

End point title	Treatment Phase: Percentage of Participants Who Discontinued Study Drug Due to Any Treatment-Emergent Adverse Event (TEAE)[4]

End point description:

An AE is any untoward medical occurrence in a clinical study participant administered a medicinal product, which does not necessarily have a causal relationship with the treatment. An AE can therefore be any unfavorable and/or unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. TEAEs were defined as 1 or both of the following: Any AEs with an onset date on or after the study drug start date and no later than 30 days after permanent discontinuation of study drug and/or Any AEs leading to premature discontinuation of study drug. The Safety Analysis Set included all participants who were enrolled into the study and received at least 1 dose of study drug (SOF/VEL FDC).

End point type	Primary

End point timeframe:

From first dose through last dose of the study drug (Up to 12 weeks) plus 30 days

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical comparison was planned or performed.

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	73	41	
Units: percentage of participants				
number (not applicable)	0.0	2.7	2.4	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Lead-in Phase: Change From Baseline in Hepatitis C Virus (HCV) Ribonucleic Acid (RNA) at Day 7

End point title	PK Lead-in Phase: Change From Baseline in Hepatitis C Virus (HCV) Ribonucleic Acid (RNA) at Day 7

End point description:

End point type	Secondary

End point timeframe:

Baseline; Day 7

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	20	19	
Units: log10 international units (IU)/mL				
arithmetic mean (standard deviation)				
Baseline	6.09 (± 0.569)	5.84 (± 0.656)	5.77 (± 1.275)	
Change from Baseline at Day 7	-4.48 (± 0.656)	-4.20 (± 0.642)	-3.94 (± 1.082)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK Lead-in Phase: Percentage of Participants Who Permanently Discontinued Study Drug Due to an Adverse (AE)

End point title	PK Lead-in Phase: Percentage of Participants Who Permanently Discontinued Study Drug Due to an Adverse (AE)

End point description:

An AE is any untoward medical occurrence in a clinical study participant administered a medicinal product, which does not necessarily have a causal relationship with the treatment. An AE can, therefore, be any unfavorable and/or unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Participants in the Lead-in Phase PK Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

First dose date up to Day 7

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	17	20	19	
Units: percentage of participants				
number (not applicable)	0.0	0.0	0.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Phase: Percentage of Participants With Sustained Virologic Response (SVR) at 12 Weeks After Discontinuation of Therapy (SVR12)

End point title	Treatment Phase: Percentage of Participants With Sustained Virologic Response (SVR) at 12 Weeks After Discontinuation of Therapy (SVR12)

End point description:

SVR12 was defined as HCV RNA < the lower limit of quantitation (LLOQ; ie, 15 IU/mL) at 12 weeks after stopping study treatment. The Full Analysis Set included all participants who were enrolled into the study and received at least 1 dose of study drug (SOF/VEL FDC).

End point type	Secondary

End point timeframe:

Posttreatment Week 12

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	73	41	
Units: percentage of participants				
number (confidence interval 95%)	95.1 (88.9 to 98.4)	93.2 (84.7 to 97.7)	82.9 (67.9 to 92.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Phase: Percentage of Participants With SVR at 4 Weeks After Discontinuation of Therapy (SVR4)

End point title	Treatment Phase: Percentage of Participants With SVR at 4 Weeks After Discontinuation of Therapy (SVR4)

End point description:

SVR4 was defined as HCV RNA < LLOQ (ie, 15 IU/mL) at 4 weeks after stopping study treatment. Participants in the Full Analysis Set were analyzed.

End point type	Secondary
End point timeframe: Posttreatment Week 4	

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	73	41	
Units: percentage of participants				
number (confidence interval 95%)	96.1 (90.3 to 98.9)	94.5 (86.6 to 98.5)	82.9 (67.9 to 92.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Phase: Percentage of Participants With SVR at 24 Weeks After Discontinuation of Therapy (SVR24)

End point title	Treatment Phase: Percentage of Participants With SVR at 24 Weeks After Discontinuation of Therapy (SVR24)
End point description: SVR 24 was defined as HCV RNA < LLOQ (ie, 15 IU/mL) at 24 weeks after stopping study treatment. Participants in the Full Analysis Set were analyzed.	
End point type	Secondary
End point timeframe: Posttreatment Week 24	

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	73	41	
Units: percentage of participants				
number (confidence interval 95%)	95.1 (88.9 to 98.4)	93.2 (84.7 to 97.7)	82.9 (67.9 to 92.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Phase: Percentage of Participants With Virologic Failure

End point title	Treatment Phase: Percentage of Participants With Virologic Failure

End point description:

Virologic failure was defined as: On-treatment virologic failure - Breakthrough (confirmed HCV RNA ≥ LLOQ after having previously had HCV RNA < LLOQ while on treatment), or Rebound (confirmed > 1 log10 IU/mL increase in HCV RNA from nadir while on treatment), or Non-response (HCV RNA persistently ≥ LLOQ through 8 weeks of treatment); Virologic relapse: Confirmed HCV RNA ≥ LLOQ during the posttreatment period having achieved HCV RNA < LLOQ at last on-treatment visit. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Up to Posttreatment Week 24

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	73	41	
Units: percentage of participants				
number (not applicable)	1.0	1.4	0.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Phase: Percentage of Participants With HCV RNA < LLOQ On Treatment

End point title	Treatment Phase: Percentage of Participants With HCV RNA < LLOQ On Treatment

End point description:

Percentage of participants with HCV RNA < LLOQ while on treatment by analysis visit. Participants in the Full Analysis Set were analyzed.

End point type	Secondary

End point timeframe:

Weeks 1, 4, 8, and 12

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	73	41	
Units: percentage of participants				
number (confidence interval 95%)				
Week 1	44.1 (34.3 to 54.3)	39.7 (28.5 to 51.9)	36.8 (21.8 to 54.0)	
Week 4	96.1 (90.3 to 98.9)	94.4 (86.2 to 98.4)	91.4 (76.9 to 98.2)	
Week 8	100.0 (96.4 to 100.0)	98.6 (92.3 to 100.0)	100.0 (89.7 to 100.0)	
Week 12	100.0 (96.4 to 100.0)	98.6 (92.3 to 100.0)	100.0 (89.7 to 100.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Phase: Percentage of Participants Who Develop Viral Resistance to SOF and/or VEL During Treatment and After Discontinuation of Treatment

End point title	Treatment Phase: Percentage of Participants Who Develop Viral Resistance to SOF and/or VEL During Treatment and After Discontinuation of Treatment

End point description:

Drug-resistant substitutions were analyzed as part of the Virology Study. Plasma samples were collected and stored for potential HCV sequencing. Impact on the treatment outcomes of SVR12 and SVR24 were observed during the study. Baseline deep sequencing of the HCV nonstructural protein (NS)5A and NS5B genes was performed for all participants at the first time point after virologic failure if the plasma or serum sample was available. Pretreatment full-length NS5A deep sequencing data were obtained at a 15% assay cutoff for the Resistance Analysis Population which covered all NS5A and NS5B nucleoside inhibitor (NI) resistance-associated variants (RAVs).

End point type	Secondary

End point timeframe:

First dose date up to Posttreatment Week 24

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	98	68	33	
Units: percentage of participants				
number (not applicable)				
Pretreatment NS5A NI RAVs	16.3	10.2	18.1	
Pretreatment NS5B NI RAVs	5.1	0.0	3.0	

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Phase: Change From Baseline in HCV RNA at Weeks 1, 4, 8, and 12

End point title	Treatment Phase: Change From Baseline in HCV RNA at Weeks 1, 4, 8, and 12

End point description:

Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Weeks 1, 4, 8, and 12

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	73	41	
Units: log10 IU/mL				
arithmetic mean (standard deviation)				
Baseline	6.06 (± 0.585)	5.87 (± 0.686)	5.86 (± 1.057)	
Change from Baseline at Week 1 (N = 102, 71, 36)	-4.46 (± 0.661)	-4.28 (± 0.632)	-4.06 (± 0.914)	
Change from Baseline at Week 4 (N = 102, 71, 34)	-4.89 (± 0.578)	-4.64 (± 0.860)	-4.49 (± 1.040)	
Change from Baseline at Week 8 (N = 101, 70, 34)	-4.91 (± 0.588)	-4.69 (± 0.678)	-4.56 (± 1.066)	
Change from Baseline at Week 12 (N = 101, 69, 34)	-4.91 (± 0.588)	-4.70 (± 0.683)	-4.56 (± 1.066)	

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Phase: Quality of Life (QoL) and Neuropsychiatric Assessments as Measured by PedsQL™ Pediatric QoL Survey

End point title	Treatment Phase: Quality of Life (QoL) and Neuropsychiatric Assessments as Measured by PedsQL™ Pediatric QoL Survey

End point description:

To evaluate the effect of treatment with SOF/VEL on general and disease-specific health-related QoL, the PedsQL™ Pediatric QoL Inventory V4.0 Short Form (SF15) was completed at Day 1 (baseline/BL), end of treatment (EOT), early termination (if applicable), and posttreatment Weeks (Wk) 12 (follow up-12/FU-12) and 24. The SF15 questionnaire represented 4 domains: physical, emotional, social, and school functioning, with the emotional, social, and school functioning domains representing the psychosocial health summary. Neuropsychiatric assessment was conducted using the PedsQL™ Pediatric QoL Inventory V4.0 SF15 psychosocial domain-related scores. Items were calculated and transformed into an overall score with a range of 0 to 100 points, with more points indicating better QoL. Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Week 12, End of Treatment (EOT), Posttreatment/Follow-up (FU) Week-12 (FU-12), and FU Week-24 (FU-24)

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	73	41	
Units: score on a scale				
arithmetic mean (standard deviation)				
Parent Reports, Total Score at BL (N=98,73,41)	80.0 (± 17.71)	79.7 (± 15.58)	86.5 (± 12.43)	
Parent Reports, Total Score at Wk 12(N=97,68,32)	82.4 (± 18.13)	82.8 (± 14.26)	87.3 (± 11.31)	
Parent Reports, Total Score at EOT (N=97,70,34)	82.4 (± 18.13)	82.2 (± 14.95)	87.0 (± 11.65)	
Parent Reports, Total Score at FU-12 (N=94,68,35)	81.7 (± 17.39)	81.5 (± 15.34)	87.7 (± 14.11)	
Parent Reports, Total Score at FU-24 (N=94,69,35)	80.8 (± 18.65)	79.7 (± 15.30)	88.3 (± 9.79)	
Part. Reports,Total Score at BL(N=100,73,18)	79.9 (± 15.22)	77.9 (± 13.33)	82.2 (± 12.47)	
Part. Reports,Total Score at Wk 12(N=101,68,21)	80.9 (± 16.38)	80.0 (± 14.21)	83.3 (± 11.62)	
Part. Reports,Total Score at EOT(N=101,70,21)	80.9 (± 16.38)	79.7 (± 14.13)	83.3 (± 11.62)	
Part. Reports,Total Score at FU-12(N=98,68,23)	82.5 (± 15.41)	81.1 (± 13.32)	80.5 (± 14.18)	
Part. Reports,Total Score at FU-24(N=98,69,25)	81.4 (± 16.34)	81.7 (± 15.43)	82.1 (± 12.56)	

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Phase: Change From Baseline in Growth and Development as Measured by Height Percentiles

End point title	Treatment Phase: Change From Baseline in Growth and Development as Measured by Height Percentiles

End point description:

An age- and sex-specific percentile was derived for each weight, height, and body mass index (BMI) measurement according to the statistical analysis system (SAS) program available on the Centers for Disease Control and Prevention (CDC) website using the year 2000 growth charts. Participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Weeks 1, 4, 8, 12, Follow-up (FU) Week 4 (FU-4), FU-12, and FU-24

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	73	41	
Units: cm				
median (inter-quartile range (Q1-Q3))				
Baseline	44.5 (16.2 to 74.1)	41.9 (20.5 to 65.2)	39.3 (13.9 to 70.1)	

Change from Baseline at Week 1 (N = 102, 73, 36)	0.0 (-0.4 to 0.9)	0.1 (-0.7 to 2.4)	0.5 (-1.1 to 3.4)	
Change from Baseline at Week 4 (N = 101, 71, 34)	0.0 (-0.7 to 1.7)	0.2 (-1.9 to 1.9)	1.4 (-0.3 to 3.7)	
Change from Baseline at Week 8 (N = 101, 69, 34)	0.0 (-1.2 to 1.5)	-0.1 (-2.2 to 2.2)	0.3 (-2.1 to 3.6)	
Change from Baseline at Week 12 (N = 100, 65, 28)	-0.1 (-1.4 to 1.0)	0.2 (-2.6 to 2.8)	0.2 (-2.0 to 5.1)	
Change from Baseline at FU-4 (N = 99, 70, 34)	0.0 (-2.0 to 1.3)	0.2 (-2.3 to 2.5)	1.2 (-0.7 to 5.6)	
Change from Baseline at FU-12 (N = 98, 68, 35)	-0.2 (-2.4 to 1.4)	0.1 (-1.7 to 2.6)	0.6 (-3.1 to 4.6)	
Change from Baseline at FU-24 (N = 91, 67, 33)	-0.6 (-2.6 to 1.9)	-0.2 (-3.1 to 3.5)	0.3 (-2.1 to 6.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Phase: Change From Baseline in Growth and Development as Measured by Weight Percentiles

End point title	Treatment Phase: Change From Baseline in Growth and Development as Measured by Weight Percentiles

End point description:

An age- and sex-specific percentile was derived for each weight, height, and BMI measurement according to the SAS program available on the CDC website using the year 2000 growth charts. Participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; Weeks 1, 4, 8, 12, FU-4, FU-12, and FU-24

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	73	41	
Units: kg				
median (inter-quartile range (Q1-Q3))				
Baseline	67.2 (31.5 to 84.1)	45.9 (23.3 to 78.6)	64.6 (38.0 to 86.7)	
Change from Baseline at Week 1 (N = 102, 73, 36)	0.0 (-0.4 to 0.9)	0.1 (-0.6 to 1.2)	-0.5 (-2.7 to 0.7)	
Change from Baseline at Week 4 (N = 102, 71, 34)	0.0 (-0.9 to 1.8)	0.2 (-1.4 to 1.5)	0.3 (-1.2 to 2.0)	
Change from Baseline at Week 8 (N = 101, 69, 34)	0.0 (-1.3 to 2.1)	0.1 (-1.6 to 2.5)	0.2 (-3.7 to 2.5)	
Change from Baseline at Week 12 (N = 100, 65, 28)	0.2 (-1.0 to 2.9)	0.5 (-1.7 to 2.5)	-1.7 (-4.7 to 0.6)	
Change from Baseline at FU-4 (N = 99, 70, 34)	0.1 (-3.0 to 3.1)	0.0 (-2.3 to 2.6)	-0.8 (-4.9 to 2.4)	
Change from Baseline at FU-12 (N = 98, 68, 35)	0.0 (-2.5 to 4.7)	0.5 (-2.2 to 4.9)	-0.8 (-6.6 to 2.2)	
Change from Baseline at FU-24 (N = 91, 67, 33)	0.1 (-2.6 to 4.1)	1.4 (-1.2 to 5.7)	-1.3 (-3.5 to 2.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Phase: Changes in Growth and Development as Measured by Tanner Stage Assessment From Baseline

End point title	Treatment Phase: Changes in Growth and Development as Measured by Tanner Stage Assessment From Baseline

End point description:

Tanner Pubertal Staging was assessed for pubic hair growth and genitalia development (males) and for pubic hair growth and breast development (females) in stages 1 to 5. Tanner stages were used to evaluate the onset and progression of pubertal changes from stage 1 (pre-pubertal) to stage 5 (adult). If a participant had reached Tanner stage 5, no further Tanner pubertal stage assessments were to be completed. Pubic hair growth: Tanner stages (1: No hair, 2: Downy hair, 3: More coarse and curly hair, 4: Adult-like hair quality; 5: Hair extends to the medial surface of the thighs); Breast development: Tanner stages (1: No glandular tissue, 2: Breast bud forms,3: More elevated, outside areola, 4: Increased breast size,5: Final adult-size breasts); Genitalia development: Tanner stages (1: Testes, scrotum, and penis about same size, 2: Enlargement of scrotum, testes and penis, 3: Enlargement of penis, 4: Penis size enlargement, 5: Genitalia adult in size and shape). Safety Analysis Set.

End point type	Secondary

End point timeframe:

Up to Posttreatment Week 24

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	73	41	
Units: participants				
Pubic Hair (Male): Baseline, Stage 1 (N=50,35,17)	4	31	17	
Pubic Hair (Male): Baseline, Stage 2 (N=50,35,17)	3	2	0	
Pubic Hair (Male): Baseline, Stage 3 (N=50,35,17)	10	1	0	
Pubic Hair (Male): Baseline, Stage 4 (N=50,35,17)	14	0	0	
Pubic Hair (Male): Baseline, Stage 5 (N=50,35,17)	19	0	0	
Pubic Hair (Male): EOT, Stage 1 (N=50,32,13)	2	28	13	
Pubic Hair (Male): EOT, Stage 2 (N=50,32,13)	4	3	0	
Pubic Hair (Male): EOT, Stage 3 (N=50,32,13)	7	1	0	
Pubic Hair (Male): EOT, Stage 4 (N=50,32,13)	13	0	0	
Pubic Hair (Male): EOT, Stage 5 (N=50,32,13)	24	0	0	

Pubic Hair (Male): FU-12, Stage 1 (N=47,30,14)	1	27	14	
Pubic Hair (Male): FU-12, Stage 2 (N=47,30,14)	5	3	0	
Pubic Hair (Male): FU-12, Stage 3 (N=47,30,14)	6	1	0	
Pubic Hair (Male): FU-12, Stage 4 (N=47,30,14)	10	0	0	
Pubic Hair (Male): FU-12, Stage 5 (N=47,30,14)	25	0	0	
Pubic Hair (Male): FU-24, Stage 1 (N=45,32,14)	1	30	14	
Pubic Hair (Male): FU-24, Stage 2 (N=45,32,14)	4	2	0	
Pubic Hair (Male): FU-24, Stage 3 (N=45,32,14)	2	1	0	
Pubic Hair (Male): FU-24, Stage 4 (N=45,32,14)	13	0	0	
Pubic Hair (Male): FU-24, Stage 5 (N=45,32,14)	25	0	0	
Genitalia (Male): Baseline, Stage 1 (N=50,35,17)	4	31	17	
Genitalia (Male): Baseline, Stage 2 (N=50,35,17)	3	2	0	
Genitalia (Male): Baseline, Stage 3 (N=50,35,17)	8	1	0	
Genitalia (Male): Baseline, Stage 4 (N=50,35,17)	16	0	0	
Genitalia (Male): Baseline, Stage 5 (N=50,35,17)	19	0	0	
Genitalia (Male): EOT, Stage 1 (N=50,32,13)	2	28	13	
Genitalia (Male): EOT, Stage 2 (N=50,32,13)	3	3	0	
Genitalia (Male): EOT, Stage 3 (N=50,32,13)	7	1	0	
Genitalia (Male): EOT, Stage 4 (N=50,32,13)	15	0	0	
Genitalia (Male): EOT, Stage 5 (N=50,32,13)	23	0	0	
Genitalia (Male): FU-12, Stage 1 (N=47,30,14)	1	27	14	
Genitalia (Male): FU-12, Stage 2 (N=47,30,14)	4	3	0	
Genitalia (Male): FU-12, Stage 3 (N=47,30,14)	7	1	0	
Genitalia (Male): FU-12, Stage 4 (N=47,30,14)	11	0	0	
Genitalia (Male): FU-12, Stage 5 (N=47,30,14)	24	0	0	
Genitalia (Male): FU-24, Stage 1 (N=45,32,14)	1	28	14	
Genitalia (Male): FU-24, Stage 2 (N=45,32,14)	2	4	0	
Genitalia (Male): FU-24, Stage 3 (N=45,32,14)	4	1	0	
Genitalia (Male): FU-24, Stage 4 (N=45,32,14)	13	0	0	
Genitalia (Male): FU-24, Stage 5 (N=45,32,14)	25	0	0	
Pubic Hair (Female): Baseline, Stage 1(N=52,38,24)	2	31	24	

Pubic Hair (Female): Baseline, Stage 2(N=52,38,24)	3	5	0	
Pubic Hair (Female): Baseline, Stage 3(N=52,38,24)	9	2	0	
Pubic Hair (Female): Baseline, Stage 4(N=52,38,24)	16	0	0	
Pubic Hair (Female): Baseline, Stage 5(N=52,38,24)	22	0	0	
Pubic Hair (Female): EOT, Stage 1 (N=50,37,21)	2	29	21	
Pubic Hair (Female): EOT, Stage 2 (N=50,37,21)	2	5	0	
Pubic Hair (Female): EOT, Stage 3 (N=50,37,21)	6	2	0	
Pubic Hair (Female): EOT, Stage 4 (N=50,37,21)	10	1	0	
Pubic Hair (Female): EOT, Stage 5 (N=50,37,21)	30	0	0	
Pubic Hair (Female): FU-12, Stage 1 (N=51,35,21)	2	24	21	
Pubic Hair (Female): FU-12, Stage 2 (N=51,35,21)	1	7	0	
Pubic Hair (Female): FU-12, Stage 3 (N=51,35,21)	8	3	0	
Pubic Hair (Female): FU-12, Stage 4 (N=51,35,21)	8	1	0	
Pubic Hair (Female): FU-12, Stage 5 (N=51,35,21)	32	0	0	
Pubic Hair (Female): FU-24, Stage 1 (N=50,35,21)	2	24	20	
Pubic Hair (Female): FU-24, Stage 2 (N=50,35,21)	0	6	1	
Pubic Hair (Female): FU-24, Stage 3 (N=50,35,21)	8	1	0	
Pubic Hair (Female): FU-24, Stage 4 (N=50,35,21)	9	4	0	
Pubic Hair (Female): FU-24, Stage 5 (N=50,35,21)	31	0	0	
Breasts (Female): Baseline, Stage 1 (N=52,38,24)	1	29	24	
Breasts (Female): Baseline, Stage 2 (N=52,38,24)	5	6	0	
Breasts (Female): Baseline, Stage 3 (N=52,38,24)	6	3	0	
Breasts (Female): Baseline, Stage 4 (N=52,38,24)	17	0	0	
Breasts (Female): Baseline, Stage 5 (N=52,38,24)	23	0	0	
Breasts (Female): EOT, Stage 1 (N=50,37,21)	1	25	21	
Breasts (Female): EOT, Stage 2 (N=50,37,21)	2	9	0	
Breasts (Female): EOT, Stage 3 (N=50,37,21)	6	2	0	
Breasts (Female): EOT, Stage 4 (N=50,37,21)	14	1	0	
Breasts (Female): EOT, Stage 5 (N=50,37,21)	27	0	0	
Breasts (Female): FU-12, Stage 1 (N=51,35,21)	1	20	21	
Breasts (Female): FU-12, Stage 2 (N=51,35,21)	2	11	0	

Breasts (Female): FU-12, Stage 3 (N=51,35,21)	5	2	0	
Breasts (Female): FU-12, Stage 4 (N=51,35,21)	15	2	0	
Breasts (Female): FU-12, Stage 5 (N=51,35,21)	28	0	0	
Breasts (Female): FU-24, Stage 1 (N=50,35,21)	1	20	20	
Breasts (Female): FU-24, Stage 2 (N=50,35,21)	0	10	1	
Breasts (Female): FU-24, Stage 3 (N=50,35,21)	6	3	0	
Breasts (Female): FU-24, Stage 4 (N=50,35,21)	13	2	0	
Breasts (Female): FU-24, Stage 5 (N=50,35,21)	30	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Growth and Development as Measured by Parental Height

End point title	Growth and Development as Measured by Parental Height

End point description:

Mid-parental height was calculated as the average of the biological father's and mother's heights. For boys, the sex adjusted mid-parental height was calculated by adding 2.5 inches or 6.5 cm to the mean of the parents' heights. For girls, 2.5 inches or 6.5 cm was subtracted from the mean of the parents' heights. Participants in the Safety Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Day 1

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	39	23	
Units: cm				
median (inter-quartile range (Q1-Q3))	170.5 (162.0 to 176.7)	170.0 (163.7 to 178.6)	168.7 (163.0 to 174.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Phase: Change From Baseline in Growth and Development as Measured by Bone Age

End point title	Treatment Phase: Change From Baseline in Growth and Development as Measured by Bone Age

End point description:

Bone age was determined based on x-ray of the left wrist, hand, and fingers. Baseline value is the last available value on or prior to first dose date of study drug. Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Baseline; FU-24

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	73	41	
Units: years				
median (inter-quartile range (Q1-Q3))				
Baseline (N = 102, 72, 40)	15.5 (13.5 to 17.0)	7.8 (6.8 to 9.0)	4.8 (4.2 to 5.5)	
Change from Baseline at FU-24 (N = 92, 68, 35)	0.6 (0.0 to 1.0)	1.0 (0.0 to 1.2)	0.5 (0.0 to 1.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Phase: Swallowability of SOF/VEL as Assessed by the Participant's Ability to Swallow SOF/VEL Placebo Tablets at Baseline

End point title	Treatment Phase: Swallowability of SOF/VEL as Assessed by the Participant's Ability to Swallow SOF/VEL Placebo Tablets at Baseline[5]

End point description:

A SOF/VEL FDC swallowability assessment was performed using placebo (PBO) tablets at baseline. Participants in the Full Analysis Set with available data were analyzed. Swallowability assessment was performed in 12 to <18 years old and 6 to < 12 Years old only.

End point type	Secondary

End point timeframe:

Baseline

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical comparison was planned or performed.

End point values	12 to < 18 Years Old	6 to < 12 Years Old		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	73		
Units: participants				
SOF/VEL 400/100mg PBO,Able to Swallow(N=102,1)	92	1		
SOF/VEL 400/100mg PBO,Not Able to Swallow(N=102,1)	10	0		
SOF/VEL 200/50mg PBO,Able to Swallow(N=10,73)	10	72		

SOF/VEL 200/50mg PBO,Not Able to Swallow(N=10,73)	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Phase: Number of Participants With Acceptability of SOF/VEL as Measured by a Questionnaire to Assess Acceptability, Including Palatability at Day 1

End point title	Treatment Phase: Number of Participants With Acceptability of SOF/VEL as Measured by a Questionnaire to Assess Acceptability, Including Palatability at Day 1

End point description:

Acceptability was assessed by numeric response marked on line between numbers 0 - 100. Higher scores indicate better acceptability and/or palatability. Participants in the Full Analysis Set with available data were analyzed.

End point type	Secondary

End point timeframe:

Day 1

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	12 to <18 Years Old
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	91	72	29	11
Units: participants				
Taste, Participants Who Did Not Taste Study Drug	61	42	8	5
Taste, Participants Who Marked > 60 to 100	16	11	6	3
Taste, Participants Who Marked 40 to 60	11	6	4	1
Taste, Participants Who Marked 0 to < 40	3	12	9	2
Easy to Take, Who Marked > 60 to 100 (N=89,71,27)	82	60	13	9
Easy to Take, Who Marked 40 to 60 (N=89,71,27)	5	3	4	1
Easy to Take, Who Marked 0 to < 40 (N=89,71,27)	2	8	10	1

End point values	6 to <12 Years Old	3 to <6 Years Old		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1	12		
Units: participants				
Taste, Participants Who Did Not Taste Study Drug	0	5		

Taste, Participants Who Marked > 60 to 100	0	3		
Taste, Participants Who Marked 40 to 60	0	1		
Taste, Participants Who Marked 0 to < 40	1	3		
Easy to Take, Who Marked > 60 to 100 (N=89,71,27)	0	4		
Easy to Take, Who Marked 40 to 60 (N=89,71,27)	0	2		
Easy to Take, Who Marked 0 to < 40 (N=89,71,27)	1	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Phase: Number of Participants With Acceptability of SOF/VEL as Measured by a Questionnaire to Assess Acceptability, Including Palatability at Week 12

End point title	Treatment Phase: Number of Participants With Acceptability of SOF/VEL as Measured by a Questionnaire to Assess Acceptability, Including Palatability at Week 12

End point description:

Acceptability was assessed by numeric response marked on line between numbers 0 - 100. Higher scores indicate better acceptability and/or palatability. Participants in the Full Analysis Set with available data were analyzed. Here, 99999 = Data not applicable for the oral granules group.

End point type	Secondary

End point timeframe:

Week 12

End point values	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old	12 to <18 Years Old
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	91	72	29	11
Units: participants				
Taste, Who Did Not Taste Study Drug(N=90,70,23)	49	33	8	2
Taste, Who Marked > 60 to 100 (N=90,70,23)	24	14	4	5
Taste, Who Marked 40 to 60 (N=90,70,23)	10	12	4	1
Taste, Who Marked 0 to < 40 (N=90,70,23)	7	11	7	3
Easy to Take, Who Marked > 60 to 100 (N=89,70,23)	83	65	20	9
Easy to Take, Who Marked 40 to 60 (N=89,70,23)	3	5	1	0
Easy to Take, Who Marked 0 to < 40 (N=89,70,23)	3	0	2	2
Feels Taking Pills, > 60 to 100 mark (N=88,70,23)	82	60	99999	8
Feels Taking Pills, 40 to 60 mark (N=88,70,23)	3	7	99999	1

Feels Taking Pills, 0 to < 40 mark (N=88,70,23)	3	3	99999	2

End point values	6 to <12 Years Old	3 to <6 Years Old		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1	12		
Units: participants				
Taste, Who Did Not Taste Study Drug(N=90,70,23)	0	2		
Taste, Who Marked > 60 to 100 (N=90,70,23)	0	1		
Taste, Who Marked 40 to 60 (N=90,70,23)	1	3		
Taste, Who Marked 0 to < 40 (N=90,70,23)	0	2		
Easy to Take, Who Marked > 60 to 100 (N=89,70,23)	1	6		
Easy to Take, Who Marked 40 to 60 (N=89,70,23)	0	1		
Easy to Take, Who Marked 0 to < 40 (N=89,70,23)	0	1		
Feels Taking Pills, > 60 to 100 mark (N=88,70,23)	99999	99999		
Feels Taking Pills, 40 to 60 mark (N=88,70,23)	99999	99999		
Feels Taking Pills, 0 to < 40 mark (N=88,70,23)	99999	99999		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events: From first dose through last dose of the study drug (Up to 12 weeks) plus 30 days; All-Cause Mortality: First dose date up to Posttreatment Week 24

Adverse event reporting additional description:

The Safety Analysis Set included all participants who were enrolled into the study and received at least 1 dose of study drug (SOF/VEL FDC).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	12 to < 18 Years Old

Reporting group description:

PK Lead-in Phase: Sofosbuvir/Velpatasvir (SOF/VEL) fixed-dose combination (FDC) 400/100 mg tablets or oral granules once daily for 7 days. Participants who completed the PK lead-in phase and other additional participants were enrolled into the treatment phase with no interruption of study drug administration until the appropriateness of the dose had been confirmed by PK and safety results from the PK lead-in phase.
Treatment Phase: SOF/VEL FDC 400/100 mg tablets or oral granules once daily for 12 weeks.

Reporting group title	6 to < 12 Years Old

Reporting group description:

PK Lead-in Phase: SOF/VEL FDC 200/50 mg tablets or oral granules once daily for 7 days. Participants who completed the PK lead-in phase, continued into the treatment phase with no interruption of study drug administration and additional participants were enrolled into the treatment phase once the appropriateness of the dose was confirmed by PK results from the PK lead-in phase.
Treatment Phase: SOF/VEL FDC 200/50 mg tablets or oral granules once daily for 12 weeks.

Reporting group title	3 to < 6 Years Old

Reporting group description:

PK Lead-in Phase: SOF/VEL FDC 200/50 mg oral granules once daily for 7 days for participants who weighed ≥ 17 kg. SOF/VEL FDC 150/37.5 mg oral granules once daily for 7 days for participants who weighed < 17 kg. Participants who completed the PK lead-in phase, continued into the treatment phase with no interruption of study drug administration and additional participants were enrolled into the treatment phase once the appropriateness of the dose was confirmed by PK results from the PK lead-in phase.
Treatment Phase: SOF/VEL FDC 200/50 mg oral granules once daily for 12 weeks for participants who weighed ≥ 17 kg. SOF/VEL FDC 150/37.5 mg oral granules once daily for 12 weeks for participants who weighed < 17 kg.

Serious adverse events	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 102 (1.96%)	2 / 73 (2.74%)	0 / 41 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Constipation			

subjects affected / exposed	0 / 102 (0.00%)	1 / 73 (1.37%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	2 / 102 (1.96%)	0 / 73 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bipolar disorder			
subjects affected / exposed	1 / 102 (0.98%)	0 / 73 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination, auditory			
subjects affected / exposed	0 / 102 (0.00%)	1 / 73 (1.37%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 102 (0.98%)	0 / 73 (0.00%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	12 to < 18 Years Old	6 to < 12 Years Old	3 to < 6 Years Old
Total subjects affected by non-serious adverse events			
subjects affected / exposed	65 / 102 (63.73%)	53 / 73 (72.60%)	26 / 41 (63.41%)
Injury, poisoning and procedural complications			
Product use issue			
subjects affected / exposed	0 / 102 (0.00%)	2 / 73 (2.74%)	4 / 41 (9.76%)
occurrences (all)	0	3	4
Nervous system disorders			
Headache			
subjects affected / exposed	30 / 102 (29.41%)	11 / 73 (15.07%)	2 / 41 (4.88%)
occurrences (all)	49	17	2

Dizziness			
subjects affected / exposed	9 / 102 (8.82%)	2 / 73 (2.74%)	1 / 41 (2.44%)
occurrences (all)	11	3	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	22 / 102 (21.57%)	9 / 73 (12.33%)	5 / 41 (12.20%)
occurrences (all)	25	9	6
Pyrexia			
subjects affected / exposed	10 / 102 (9.80%)	8 / 73 (10.96%)	6 / 41 (14.63%)
occurrences (all)	10	9	8
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	9 / 102 (8.82%)	12 / 73 (16.44%)	11 / 41 (26.83%)
occurrences (all)	11	13	15
Nausea			
subjects affected / exposed	17 / 102 (16.67%)	5 / 73 (6.85%)	0 / 41 (0.00%)
occurrences (all)	18	5	0
Diarrhoea			
subjects affected / exposed	7 / 102 (6.86%)	6 / 73 (8.22%)	5 / 41 (12.20%)
occurrences (all)	7	7	6
Abdominal pain			
subjects affected / exposed	6 / 102 (5.88%)	9 / 73 (12.33%)	2 / 41 (4.88%)
occurrences (all)	7	11	4
Abdominal pain upper			
subjects affected / exposed	10 / 102 (9.80%)	3 / 73 (4.11%)	2 / 41 (4.88%)
occurrences (all)	11	5	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 102 (9.80%)	11 / 73 (15.07%)	6 / 41 (14.63%)
occurrences (all)	10	15	8
Nasal congestion			
subjects affected / exposed	6 / 102 (5.88%)	4 / 73 (5.48%)	5 / 41 (12.20%)
occurrences (all)	8	5	5
Rhinorrhoea			
subjects affected / exposed	4 / 102 (3.92%)	4 / 73 (5.48%)	6 / 41 (14.63%)
occurrences (all)	4	4	7

Epistaxis			
subjects affected / exposed	3 / 102 (2.94%)	6 / 73 (8.22%)	2 / 41 (4.88%)
occurrences (all)	3	9	2
Oropharyngeal pain			
subjects affected / exposed	9 / 102 (8.82%)	2 / 73 (2.74%)	0 / 41 (0.00%)
occurrences (all)	9	2	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 102 (0.00%)	7 / 73 (9.59%)	1 / 41 (2.44%)
occurrences (all)	0	7	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 102 (0.98%)	4 / 73 (5.48%)	0 / 41 (0.00%)
occurrences (all)	1	4	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 102 (5.88%)	7 / 73 (9.59%)	1 / 41 (2.44%)
occurrences (all)	7	7	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 102 (2.94%)	7 / 73 (9.59%)	2 / 41 (4.88%)
occurrences (all)	3	8	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 102 (0.98%)	2 / 73 (2.74%)	3 / 41 (7.32%)
occurrences (all)	1	2	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 September 2016	• Added clarification that all adverse events (AEs) were recorded with a focus on those AEs leading to study drug discontinuation for evaluation of the primary safety endpoint • Updated the SOF/VEL stopping criteria to align with the LDV/SOF and SOF laboratory stopping criteria in adult and pediatric clinical studies • Added eligibility criteria pertaining to liver enzymes and bilirubin to align with the exclusion criteria parameters in SOF/VEL adult clinical studies • Clarified that only the subject was required to complete the acceptability questionnaire at Day 1, but it may be completed by the parent or legal guardian if the subject is unable to read • Clarified that the Day 3 study visit was performed over the phone and the site assessed the subject's dosing compliance by reviewing the dosing diary remotely with the subject, parent, or legal guardian • Added SOF/VEL Acceptability Questionnaire assessment to the early termination visit • Appendix 3 (Management of Clinical and Laboratory AEs) was removed due to a discrepancy in the protocol stopping rules within the protocol
01 December 2016	• Added serial hepatitis B virus (HBV) DNA monitoring for any subject with hepatitis B core antibody (HBcAb)-positive status at screening, per a US Food and Drug Administration Drug Safety Communication • Added formulation, packaging, labeling, storage, and handling information for the SOF/VEL 200/50 mg and placebo tablets
31 August 2017	• Added clinical pharmacology data and safety results from Cohort 1 from the PK lead-in phase supporting the dose for subjects 12 to < 18 years old (Group 1) in the treatment phase and dose determination for Cohort 2 (6 to < 12 years old) in the PK lead-in phase • Added an optional intensive PK substudy for adolescent subjects 12 to < 18 years old enrolled in the treatment phase at Weeks 4 or 8 to support development of the population PK model • Added additional time points to the intensive PK assessment for Cohort 3 (subjects 3 to < 6 years old) to support characterization of PK of all analytes in the youngest age group • Added clarification of the sparse PK sample at Weeks 1, 4, 8, and 12 • Added a second sparse PK sample at Weeks 4 and 8 for all enrolled subjects • Clarified that the non-tablet formulation information would be included in a future protocol amendment once it was available and would be submitted for approval prior to dosing of subjects • Added biomarker testing to align with the Gilead Sciences (Gilead) protocol template • Updated the dosing instructions in the case of vomiting to align with the SOF/VEL label • Updated the background information to include Studies GS-US-342-1553 and GS US 342 1146 since both of these studies were not included in the SOF/VEL investigator's brochure (IB)

15 June 2018	• Added clinical pharmacology data from Cohort 2 from the PK lead-in phase supporting the dose for subjects 3 to < 6 years old (Cohort 3) in the PK lead-in phase • Added dosing instructions for subjects 3 to < 6 years old • Added information on the oral granule formulation, including the dose for each age group and dosing instructions • Added subject dosing diary for subjects who were administered oral granules • Clarified dosing instructions for subjects 6 to < 12 years old • Clarified collection of parental height • Clarified requirements for the complete and symptom-directed physical examinations • Updated the disallowed and concomitant medication table to align with the table in the SOF/VEL FDC IB (Edition 5.0; dated 12 December 2017) • Updated the list of PK parameters to align with regulatory commitments • Updated the schedule of assessments for consistency

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported